Application No.: 10/607,571
Reply to Office action of April 6, 2006

Remarks/Arguments

Claims 140 and 153 have been amended. Claims 145, 151, 152, 154 and 155 are canceled. Claims 140-144, 146-150, 153-173 are pending in the application. Support for the amendments to the claims may be found, for example, at page 54, line 30; page 56, lines 6-10; and page 57, line 9. No new matter is added by the amendments.

Applicants' attorney thanks Examiner Alstrum-Acevedo and Examiner Qasi for the courtesy of a telephone interview held on July 6th, 2006. The following discussion addresses each rejection and objection set forth in the Office Action as well as certain points raised during the telephone interview.

Rejection Under 35 U.S.C. §102(e)

Examiner rejected Claims 140-144, 154 and 156-160 under 35 U.S.C. §102(e) as being anticipated by Tarara et al. (US 2005/0074498) "Tarara". The amended claims are directed to methods of administering spray-dried particles to the respiratory system of a patient, in a single, breath-actuated step. In accordance with the present claims, the particles administered to the patient comprise at least 50 micrograms of epinephrine, have a tap density of less than 0.4 g/cm^3 and have a fine particle fraction of less than 5.6 microns of at least about 45%.

In the Office Action, the Examiner highlights disclosed ranges for various features of the particles disclosed by Tarara including fine particle fractions, drug loads, tap densities, and data from cascade impactor studies of exemplary particulate compositions prepared by Tarara. The Examiner asserts that the epinephrine particles of the invention fall within the ranges disclosed by Tarara and are therefore anticipated. Applicants respectfully disagree.

For a reference to be anticipating, each and every claim limitation as set forth in the claim must be found in a single prior art reference. *Verdegaal Bros. v. Union Oil Co. of California*, 814 F.2d 628, 631 (Fed. Cir. 1987). In general, it is well accepted that a broad generic disclosure is insufficient to provide an anticipating disclosure. Where "it is necessary to select portions of teachings within a reference and combine them, e.g. select various substituents from a list of alternatives given for placement at specific sites on a generic chemical formula to arrive at a specific composition, anticipation can be found if the classes of substituents are sufficiently limited or well delineated. MPEP Section 2131.02, citing *Ex parte A*, 17 USPQ 2d 1716 (BPAI

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1990). The MPEP goes on to discuss *In re Petering*, 301 F.2d 676 (CCPA 1962). In that case, it was held that the broad generic disclosure was insufficient to anticipate the claimed compounds in view of the six variables (note that five of the variables were each selected only from hydrogen and alkyl) as a nearly infinite number of compounds were potentially claimed. The anticipating disclosure relied upon the fact that the *preferred* subgenus narrowed three of the variables to a single option, i.e., hydrogen, two variables to two options, i.e. hydrogen or methyl, and the sixth variable to one of eight groups. Only *twenty* compounds were found to be embraced by the preferred subgenus. Where, as here, the reference does not offer any guidance to choose among long lists and various ranges, anticipation cannot be found, particularly where the selection requires selecting outside the preferred embodiments. Indeed, a broad generic disclosure is often insufficient to establish that a claim is obvious. *In re Baird*, 16 F.3d 380 (Fed. Cir. 1994). As will be described below, the broad generic disclosure of this patent does not lead one of ordinary skill in the art to select the specific combination of the claimed invention.

Tarara only generically discloses products which contain epinephrine as part of a very long list of possible active agents that can be formulated. Tarara does not identify epinephrine as a preferred active agent. Tarara does not disclose or suggest the delivery of epinephrine or any other drug as a single, breath-activated step. With respect to Claims 142 and 143, for example, Tarara does not teach the desirability to formulate epinephrine in an amount between 1 and 45 or 1 and 30% by weight. Paragraph [0068] states that, more preferably, the formulations contain at least 50% active agent, (e.g. more than 90%). While it is also true that the more preferred formulations also contain more than 50%, such as more than 95%, surfactant [0061] and it is impossible for these more preferred embodiments to contain more than 100% by weight of total excipients, these conflicting teachings suggest to the person of skill in the art that these incremental ranges of every 5% are not teaching a truly preferred embodiment for any particular active agent but are merely arbitrary values added into the specification. With respect to Claim 156, the reference does not teach the desirability to target epinephrine to *both* the central airways and deep lung, nor does it teach the targeting of the individual sites (Claims 157 and 158). Nor does the reference teach the desirability of combining both local and systemic activity (Claims 159 and 160). Thus to arrive at the presently claimed formulation it becomes necessary to pick and choose amongst multiple variables and, as such, Tarara is insufficient to support an anticipation

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rejection of any one of Claims 140-144, 154, and 156-160. See MPEP 2131.02 and the cases cited therein.

Withdrawal of the rejection is respectfully requested.

Rejection Under 35 U.S.C. §103(a)

Claims 152-153 and 155 have been rejected under 35 USC 103(a) as being unpatentable over Tarara (US2005/0074498). The Examiner states that Tarara does not anticipate claims 152-153 because Tarara does not expressly teach the dosage amounts recited in the claims administered in a single inhalation. The Examiner asserts that Tarara implicitly teaches administration of particles comprising epinephrine in a single inhalation because Tarara teaches that a unit dose container in a DPI may contain from 5 to 15 mg of dry powder, corresponding to a drug loading range from 25 to 500 micrograms per dose. The Examiner further asserts that one dose comprises a single inhalation because the actuation step in the use of a dry powder requires a patient to inhale the medical composition from the DPI. The Examiner is incorrect.

The Examiner has provided no basis for concluding that a generic teaching that a unit dose container in a DPI which may contain from 5 to 15 mg of dry powder, whether or not it contains a drug load of 25-500 micrograms, teaches the desirability to deliver at least 50 micrograms of **epinephrine** in a single breath. The actual dose per actuation will depend upon a variety of factors such as the amounts of active agent and the excipients, the product morphology, and the inhaler used. The Examiner has also provided no evidence that Tarara actually delivers at least 50 micrograms of any drug, including epinephrine, to a patient in a single inhalation. In Example XXI, for example, Tarara states that the BDP powder dose delivered to the relevant stages of the cascade impactor is "77 micrograms per actuation". See, paragraph 0318 of Tarara. However, in paragraph 0315, Tarara states that there were twenty actuations. Thus if 300 micrograms of spray dried microspheres were loaded into the inhalation device as stated by Tarara in paragraph 0314, it is not possible that the FPD was 77 micrograms per actuation as 77 micrograms per actuation multiplied by 20 actuations would exceed the total number of micrograms of spray-dried powder initially loaded into the inhaler for delivery. Likewise, if 100% of the drug was delivered over 20 actuations, the amount of drug per actuation could not exceed 50 micrograms. Clearly, something is wrong with the data provided in Tarara's examples on its face. It is impossible to tell from the

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data presented in Tarara whether at least 50 micrograms of BDP or for that matter, any other drug including epinephrine, was actually delivered in a single, breath-actuated step.

The quoted sentence is not consistent with other passages of the specification. If the inhaler is loaded with 15 mg of product, which "corresponds to a drug loading ... of 25 to 500 μg per dose." The preferred embodiments possess at least 50% weight active agent. Thus, of a 15 mg product, 7.5 mg is active agent. If one assumes the 500 μg dose, for example, refers to the amount of drug delivered, (irrespective of the number of actuations required to deliver the drug) then the respirable portion of the product must be far less than that required by the claim. The product cannot have a fine particle fraction of at least about 45%. If one assumes the 500 μg to be the amount of active agent in the inhaler of the 15 mg of product, the drug load is only about 3.3%, well below the preferred ranges. The highest drug load taught here is 10% (500 μg of 5 mg), again far below the most preferred ranges. In short, these numbers, like other numbers in the patent application, appear to be arbitrary and cannot be said to provide any meaningful teaching with respect to how one would deliver an effective dose of epinephrine.

During the interview, there was a discussion as to whether Tarara's inconsistent data would still be deemed a "teaching" of the presently claimed range of 50 micrograms. Applicants' submit that if the data in Tarara is inconsistent and confusing, such data can not be deemed by one skilled in the art to be a teaching of any kind, much less that 50 micrograms of epinephrine can be delivered in a single, breath-activated step.

During the interview, the Examiner pointed to a disclosure in Tarara which states "[c]urrently, bulk reservoir type DPIs can meter between 200 micrograms and 20 mg powder per actuation". The Examiner asserted that this statement was a teaching that a powder is delivered to the patient within the presently claimed dosage range in a single, breath-activated step. This is not the case. A bulk reservoir DPI that can actuate between 200 micrograms and 20 mg of powder per actuation is not equivalent to 50 micrograms of powder *delivered* to the patient in a single, breath-actuated step. As defined in the application, the term "single, breath-actuated step" means that the particles are dispersed and inhaled in one step wherein the energy for the dispersion is provided solely by the patient. See, page 57, lines 6-24 of the present specification. Examples of suitable, single, breath activated inhalation devices are listed on page 57, lines 14-21 of the present specification. Bulk reservoir type DPI inhalers generally rely on additional energy other than the

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energy supplied solely by the patient's breath. U.S. Patents 5,458,135 and 5,997,848, owned by the same assignee as Tarara, disclose such inhalers (Exhibits A and B). The device described in 5,458,135 takes dry powder from a powder reservoir and draws it into an air stream using a dispersion nozzle. Even though the patient *may* inhale the entire dosage in a single breath, this procedure is not the same as a single-breath activated step as defined in the present specification.

The Examiner has not met his burden of showing that the present claims are obvious in view of the cited art. Even if Tarara taught all of the individual components of the present claims, there is no teaching or suggestion that would motivate or lead one skilled in the art to select the specific combination or the specific delivered doses and fine particle fractions of the present claims.

To establish a *prima facie* case of obviousness, there must be a reasonable likelihood of success for a claimed combination *In re Vaeck*, 947 F.2d 488, 20 USPQ 2d 1438 (Fed. Cir. 1991). Additionally, a reference that generically describes various elements of the claims does not *per se* establish that the claims are obvious under 35 U.S.C. 103. See *In re Baird*, 16 F.3d 380, 382; 29 USPQ2d 1550 (CCPA 1979). The Examiner has not provided any motivation as to why one skilled in the art would combine epinephrine (mentioned in a long list in Tarara), with a single, breath-actuated DPI inhaler and expect to deliver with high efficiency, 50 micrograms of epinephrine to a patient who is in need of epinephrine, likely to be in severe respiratory distress. It is noted that DPIs of any type were viewed in the art to have many drawbacks related to their reliance on inspired air from the patient. See for example column 1, lines 51-57 of Exhibit A (U.S. Patent No. 5, 458,135) where the many disadvantages of DPI's are described. Without the benefit of hindsight in view of the present invention, one skilled in the art would not be motivated to rely on a breath-actuated dry powder inhaler to deliver a life saving drug in a crisis situation that also involved difficulty in breathing. At best, if one were to attempt delivering epinephrine to a patient according to the teachings of Tarara, one would select the preferred MDIs or bulk reservoir DPIs. Even in this embodiment, one would not necessarily expect that the efficiency of delivery would be at least 50%. Yet, as disclosed in the present examples page 92, lines 8-16, T_{max} and C_{max} were *superior* to injection using the EpiPen® and standard IM injection. Given the teachings in the art that would discourage administering such drugs with these inhalers, this is a truly unexpected result.

In view of the above discussion, withdrawal of the rejection is respectfully requested.

The Examiner has rejected claims 161-162 under 35 U.S.C. §103(a) as being unpatentable over Tarara in view of the 56th edition (2002) of the Physicians Desk Reference (PDR, page 1236). Applicants respectfully disagree. Claims 161 and 162 depend from claim 140 and include all of the features of claim 140. Given the discussion of Tarara above, the PDR does not provide what Tarara lacks. While the PDR may teach that epinephrine is used to treat anaphylaxis, for example, it does not teach that patients suffering from this condition should be treated via a breath actuated inhaler with excellent efficiency and immediate results. Accordingly, Applicants respectfully request that the combination of Tarara and the PDR be withdrawn.

Claims 140-143, 146-151, 159, 160 and 162 are rejected under 35 U.S.C. §103(a) as being unpatentable over Foster (US 2003/0215512) in view of Tarara (US 2005/0074498). The Examiner states that Foster teaches a composition that comprises a mixture of pharmaceutically acceptable glassy matrix and at least one pharmacologically active material within the glassy matrix which may further be mixed with a powdered pharmaceutically acceptable carrier. The Examiner asserts that Foster discloses particles having an MMAD of about 1-5 microns, % by weight of active ingredient in a unit dosage of about 0.05% to about 99%. The Examiner further asserts that Foster discloses adrenaline, leucine, sodium tartrate and lactose from a list of actives and glass formers. The Examiner acknowledges that Foster lacks the teaching of compositions having a tap density of less than 0.4g/cm^3. However, the Examiner asserts that it would have been obvious to a person of ordinary skill in the art at the time of the instant application to combine the teachings of Foster and Tarara because both inventors teach compositions suitable for inhalation pulmonary administration of active agents, including adrenaline. The Examiner further states that the skilled artisan would have been motivated to combine the teachings of Foster and Tarara because Tarara's compositions provide teachings of desirable physical characteristics of aerodynamically light particles suitable for administration. The Examiner argues that the skilled artisan would have a reason to expect success because both references teach adrenaline compositions for inhalation.

To establish a *prima facie* case of obviousness, the prior art reference (or references when combined) must teach or suggest all of the claim limitations. There must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of

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ordinary skill in the art, to modify the reference or to combine reference teachings. There must also be a reasonable expectation of success. *See* M.P.E.P. §§2143. The teaching or suggestion to make the claimed combination and the reasonable expectation of success must both be found in the prior art, not in Appellant's disclosure. *In re Vaeck*, 947 F.2d 488 (Fed. Cir. 1991). Thus, "particular findings must be made as to the reason the skilled artisan, with no knowledge of the claimed inventions, would have selected these components for combination in the manner claimed." *In re Kotzab*, 217 F.3d 1365, 1371 (Fed. Cir. 2000). "The factual inquiry whether to combine references must be thorough and searching. It must be based on objective evidence of record. This precedent has been reinforced in myriad decisions, and cannot be dispensed with." *In re Sang Su Lee*, 277 F.3d 1338, 1343 (Fed. Cir. 2002) (citations and quotes omitted). Additionally, it is now well-established that "[b]road conclusory statements regarding the teaching of multiple references standing alone are not 'evidence'." *In re Kotzab*, 217 F.3d at 1370. "Th[e] factual question of motivation is material to patentability and [can] not be resolved on subjective belief and unknown authority." *In re Sang Su Lee*, 277 F.3d at 1343-44.

Applicants submit that the presently claimed invention recites treating a patient in need of epinephrine by administering in a single, breath-activated step, particles comprising at least 50 micrograms of epinephrine having a tap density of less than 0.4 g/cm^3 and that possess a fine particle fraction of less than 5.6 microns of at least about 45 %. While both Foster and Tarara mention adrenaline (epinephrine) as part of a long list of actives, the mere fact that both references disclose overlapping lists of active agents for incorporation of particles does not provide the skilled practitioner with an expectation of successfully mixing and matching the excipients, actives and physical properties of the particles for the purpose of successfully treating a patient in need of epinephrine. Neither reference discloses or suggests the desirability of producing an epinephrine formulation in particular having the properties as are presently claimed nor has the Examiner provided any evidence that would motivate the skilled practitioner to combine the teachings of Foster and Tarara in order to prepare spray-dried epinephrine containing particles. The Examiner has merely concluded that because both references mention both "particles" and "adrenaline" that they should be combined. This is contrary to the case law.

As discussed above, it was unexpected that inhalation of epinephrine-containing spray-dried particles would have a therapeutic effect at least as good if not better than epinephrine

delivered by intravenous injection or intramuscular injection. See Example 15 of the present specification (page 92 lines 8-16), where it is stated that the T_{max} was noticeably shorter following administration of dry powder inhalable epinephrine by inhalation as compared to intramuscular injection of epinephrine using an EpiPen®. In addition, the variability of C_{max} and T_{max} was unexpectedly reduced with the dry powder epinephrine of the invention relative to injection (page 91, lines 15-17). Indeed, it would have been totally unexpected that a person experiencing asthma or anaphylaxsis **and** who was having trouble breathing, could be effectively treated with a single inhalation from a breath-actuated dry powder inhaler of the epinephrine particles of the present invention. Like Tarara, at paragraph [0100], Foster teaches the use of the inhalers of its assignee for delivery (Exhibit C). The Examiner has provided no evidence which suggests that given both Tarara and Foster that one should expect successful treatment of asthma, anaphylaxis or any other condition characterized by bronchoconstriction, gagging and overall difficulty breathing by administering to a patient in a single breath (likely a weak breath), an effective amount of spray-dried particles to relieve the condition. The present invention is counterintuitive to the standard in the art at the time which was to deliver adrenaline to the distressed patient I.M. or I.V.

Neither Tarara nor Foster when taken alone or in combination disclose or suggest that epinephrine could be delivered in a single breath and provide all of the above-described advantages nor has the Examiner provided any motivation for one to choose epinephrine particles out of the list of active agents provided in both references. In view of the above discussion, withdrawal of the rejection is respectfully requested.

The Examiner has rejected claim 171 under 35 U.S.C. §103(a) as being unpatentable over Tarara et al as applied to claims 152, 153 and 155 above in view of Radhakrishnan (U.S. Pat. No. 5,049,389). The Examiner has also rejected claims 163-170 under 35 U.S.C. §103(a) as being unpatentable over Tarara in view of Warren et al. The above two rejections have used Tarara as the primary reference as applied to independent claim 140. For the reasons discussed above, Tarara does not teach or suggest the present claims therefore the Examiner's reliance on the teachings of the secondary references is rendered moot.

With regard to Radhakrishnan, the Examiner states that it would have been obvious to combine the teaching of Tarara and Radhakrishnan, because both inventors teach particulate compositions comprising epinephrine intended for inhalation administration. The Examiner

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further asserts that the skilled person would have been motivated to combine the teachings of Tarara and Radhakrishnan to obtain sustained release compositions which do not undergo sedimentation. The Examiner asserts that one would have a reasonable expectation of success in combining Tarara and Radhakrishnan because both inventors teach particulate compositions for the inhalation comprising adrenaline. For all of the reasons described with regard to the Examiner's combination of Foster and Tarara, the skilled practitioner would not have been motivated to choose adrenaline from amongst the many active agents listed in both Radhakrishnan and Tarara because it was counterintuitive to choose an inhalation therapy from a patient suffering from a condition in which taking a breath was difficult. Furthermore, the problem that Radhakrishnan wishes to solve (sedimentation on resuspension) is a problem encountered upon using a liquid-based nebulizer, not a dry powder inhaler. As such, one of ordinary skill in the art would not combine these two references and arrive at the claimed method which relies upon the use of a DPI. Withdrawal of the rejection is respectfully requested.

With regard to Tarara in combination with Warren, neither reference discloses an effective amount of epinephrine to be delivered in a single breath. Warren's administration of a 3 milligram dose of adrenaline in ***30 puffs*** can not be extrapolated to an administration of a formulation such as that which is presently claimed and which Tarara does not teach, suggest or disclose, because the blood plasma levels will depend not only on the amount of drug in the powder and the number of inhalations achieved but the efficiency of the delivery. Thus Warren's teachings could not be meaningfully combined with Tarara's to arrive at the present claims. Tarara does not make an adrenaline formulation and thus provides no teaching that would enable one to predict that Tarara's pharmaceutical formulations would result in maximal adrenaline blood serum levels in a shorter period of time when compared to non-intravenous routes of adrenaline administration.

The Examiner has rejected claims 172 and 173 under 35 U.S.C. §103(a) as being unpatentable over Foster in view of Tarara as applied to claims 140-143, 146-151, 159, 160, and 162 above and further in view of the Drug Information Handbook ("DIH"). Applicants respectfully disagree.

The Examiner states that the use of epinephrine bitartrate would have been apparent to a skilled artisan because it is one of the most common salts of epinephrine employed in pharmaceutical formulations. The Examiner further asserts that the person of skill would have had

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a reasonable expectation of upon combination of the cited references because all of the references teach compositions wherein the active is epinephrine and the bitartrate salt of adrenaline is commonly used in pharmaceutical formulations. For the reasons discussed above, the combination of Foster in view of Tarara does not make obvious the presently claimed invention. The DIH does not provide what the combination of Foster and Tarara lack.

Even with the above notwithstanding, the specific formulations are not reasonably taught by Foster. Foster teaches a nearly infinite number of possible combinations of a large number of active agents and a large number of excipients. There is no guidance within this broad generic disclosure to couple epinephrine bitartrate, leucine and sodium tartrate in the specific amounts claimed. The preferred active agents of Foster appear to be proteins, polypeptides and other macromolecules. Although small molecule drugs are also described and may be "adrenalin," salts thereof are not specifically disclosed. It is noted that salts of many drugs are described in the same list. The excipients of Foster span several columns. The amount of any one excipient is not described in a meaningful way to suggest a preferred amount as the teachings are limited to 3% to 99.8% by weight [paragraph [0079]. Turning to the working examples for meaningful guidance, 66.2% mannitol, 13.1% sodium citrate and 0.7% citric acid was used with 20% zinc-insulin in Example 1; 18.2% mannitol, 59.1% sodium citrate, 0.1% citric acid and 2.6% glycine was used with 20% zinc-insulin in Example 2; 10.1% mannitol, 27.1% sodium citrate, 0.2% sodium ion and 2.6% glycine was used with 60% zinc-insulin in Example 3; 18.3% mannitol, 19.0% sodium citrate, 0.2% sodium ion and 2.6% glycine was used with 60% zinc-insulin in Example 4; 77.3% sodium citrate, 0.1% citric acid and 2.6% glycine was used with 20% zinc-insulin in Example 5; and so on. Not one example employs an amino acid at high concentrations; not one example employs either leucine or sodium tartrate; not one example employs epinephrine, much less epinephrine bitartrate. A sugar is present in almost every working example. The vast majority of the working examples formulate a protein or peptide. Albuterol sulfate, the only small molecule exemplified, was formulated with 95% or 98% lactose. There is simply no motivation in this exceedingly broad disclosure of a nearly infinite number of possible combinations to select the specific excipients, in the specific amounts and combine them with epinephrine. More is required to support a *prima facie* case of obviousness than the mere fact that the words of the claim can be found within reference and the unsupported assertion that the rest that is missing from the

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reference is mere routine optimization. See *In re Baird*, 16 F.3d 380, 382; 29 USPQ2d 1550 (CCPA 1979). Applicants respectfully request withdrawal of the rejection.

Double Patenting

The Examiner has maintained the provisional rejection of claims 140-143, 151, 154, 159, and 160 under the judicially created doctrine of obviousness-type double patenting over US Application 10/818,902 ('902 application) in view of Maa. The present application claims priority to the '902 patent. In maintaining the rejection, the Examiner states that both the instant application and the copending '902 application have claims drawn to hormone active agents and a tap density of less than 0.4 g/cm^3. However, the present application does not include a single claim in which the term "hormone" is used. The presently claimed invention is drawn to particles comprising a specific active ingredient, epinephrine. While the claims of the '902 application may broadly include the particles of the present invention, the claims of the '902 application are NOT identical to the present claims in subject matter or scope. The relationship between the claims of the '902 application and the claims of the present application may be viewed as a genus-species relationship. It is well established that species claims may be separately patentable in view of the genus claims. As discussed in 3A-9 Chisum on Patents § 9.03, in *In re Kaplan*, 89 F.2d 1574, 229 USPQ 678 (Fed. Cir. 1986), the Federal Circuit held that a double patenting rejection cannot be justified solely on the ground that the subject matter of a claim in a second patent or patent application is "dominated" by the claims in a first patent.

> "By domination we refer, in accordance with established patent law terminology, to that phenomenon, which grows out of the fact that patents have claims, whereunder one patent has a broad or 'generic' claim which 'reads on' an invention defined by a narrower or more specific claim in another patent, the former 'dominating' the latter because the more narrowly claimed invention cannot be practiced without infringing the broader claim. ... In possibly simpler terms, one patent dominates another if a claim of the first patent reads on a device built or process practiced according to the second patent disclosure. This commonplace situation is not, per se, double patenting ..." 789 F.2d at 1578, 229 USPQ at 681.

The court stressed that to establish "obviousness-type" double patenting as to an attempt to obtain a patent on a variation of an invention claimed in a prior patent, there must be some clear evidence to establish why the variation would have been obvious.

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See also Eli Lilly and Co. v. Zenith Goldline Pharmaceuticals, Inc., 364 F. Supp.2d 820, 910 (S.D. Ind. 2005) ("Domination in patent law is a situation in which one patent has a broad, or generic, claim which embraces the subject matter claimed in a later, and narrower, patent. The first patent therefore 'dominates' the latter 'because the more narrowly claimed invention cannot be practiced without infringing the broader claim.' *In re Kaplan*, 789 F.2d 1574, 1577 (Fed. Cir. 1986). 'This commonplace situation is not, per se, double patenting.' *Id.* at 1577-78."; "So long as the later patent meets all of the requirements of patentability, including novelty and nonobviousness, it can properly coexist with the earlier-expiring dominant patent, and 'domination is an irrelevant fact.' *Id.* at 1578."; "Although the doctrine of double patenting prevents 'unjustified timewise extension of the right to exclude granted by a patent,' *Eli Lilly & Co.*, 251 F.3d at 968, there is no unjustified extension when the patented improvement invention is not obvious."); Pharmacia & Upjohn Co. v. Ranbaxy Pharmaceuticals, Inc., 274 F. Supp.2d 597, 610 (D. N.J. 2003), *aff'd in part, vacated in part*, 85 Fed. Appx. 205 (Fed. Cir. 2003) (nonprecedential) (citing *Kaplan*: "where the later-issued patent does not preclude the public from making compounds claimed in the earlier issued patent, there can be no finding of double patenting."). Applicants have described many of the unexpected advantages of the present epinephrine formulation above. Maa also does not disclose or suggest the specific epinephrine-containing particles of the present invention as Maa is directed to proteins and Maa also does not teach spray-dried particles as is presently claimed. Thus Maa does not provide what the claims of the '902 application lacks regarding the presently claimed epinephrine formulations. Therefore, the combination of Maa with the '902 also does not make the present claims obvious in view of the '902 patent application. In view of the above discussion, withdrawal of the rejection is requested.

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CONCLUSIONS

In view of the above amendments and remarks, it is believed that all claims are in condition for allowance, and it is respectfully requested that the application be passed to issue. If the Examiner feels that a telephone conference would expedite prosecution of this case, the Examiner is invited to call the undersigned at (978) 251-3509.

Respectfully submitted,

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